RESEARCH ARTICLE

Clinico-Morphological Profile and Receptor Status in Breast Cancer Patients in a South Indian Institution

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Abstract

Background: Breast cancer is the most common malignancy in women worldwide and the second most common cancer in females in India. Receptor status may be important for survival. Objective: To analyse and correlate the clinical and morphological parameters with receptor status in breast carcinoma patients in a tertiary care institution in Southern India. Materials and Methods: This retrospective study involved 320 patients of breast cancer diagnosed in an oncology hospital over a period of 3½ years. Data was analysed using SPSS Version 21. Results: Some 60.6% patients with breast carcinomas belonged to the age group of 40 to 60 years. The most common histological type was infiltrating ductal carcinoma, not otherwise specified, accounting for 84.4% of patients. On immunohistochemistry, estrogen receptor (ER) and progesterone receptor (PR) were expressed in 56.3% and 53.1% of cases, respectively. Conclusions: Breast cancers in India, a developing country, occur in younger women and tend to be more aggressive with lower rates of ER and PR expression and higher histological tumor grades. Both ER and PR status of the tumors had significant associations with the patient age, pathological TNM stage and histological tumor grade.

Keywords: Breast cancer - estrogen receptor - progesterone receptor - stage - grade - India

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Introduction

Breast carcinoma is the most common malignancy in females worldwide (Siegel et al., 2014). It is a leading cause of death in women (Sin ghai R et al., 2011). At many parts of India, breast carcinoma has now become the most common malignancy replacing cervical cancer, especially in urban India (Murthy et al., 2009).

Breast cancer has many clinical and morphological parameters which alter the prognosis of these patients like gross tumor size, lymph node metastases, histological grade of tumor, tumor necrosis and lymphovascular space invasion (LVSI).

Immunohistochemistry plays a very important role in the prognostication and treatment determination of breast carcinoma patients. But, due to the high cost and decreased availability of these investigations in Indian scenario, it is not routinely carried out in all centres in India.

The current study was initiated to analyse the clinical parameters, morphological profile and hormone receptor status in our breast cancer patients. The estrogen receptor (ER) and progesterone receptor (PR) status were also correlated with the clinico-morphological parameters.

Materials and Methods

The present study is a retrospective study on breast cancer patients being treated in a tertiary care oncological institute in South India from January 2011 to June 2014. Patients with a histopathologically confirmed diagnosis of breast carcinoma with immunohistochemistry report of ER and PR were included in this study after informed consent. Patients treated with neoadjuvant chemotherapy and patients with distant metastatic disease at presentation were excluded from the study. In the given time frame, 320 patients satisfied our study criteria. Institutional ethical committee approval was taken.

All mastectomy specimens were fixed in formalin and histopathological examination of paraffin embedded tissues were done after staining with haematoxylin and eosin. Histopathological tumor grading was done using the Elston and Ellis modification of the Scarff Bloom Richardson scoring (Elston and Ellis, 1991). TNM staging was done as per the American Joint Committee on Cancer (AJCC) 7th edition (Edge et al., 2010).

The status of ER and PR were obtained purely on the basis of immunohistochemical staining using standard techniques. ER or PR was considered to be positive if more than or equal to 1% tumor cell nuclei were immunoreactive.

Age, sex, tumor site, breast involved, tumor size, T stage, lymph nodal involvement, TNM stage, histological type, histological grade, lymphovascular invasion (LVSI), tumor necrosis and postoperative margin status were noted

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along with the ER and PR status of the breast carcinoma on a proforma.

Statistical analysis:-Data was tabulated in Microsoft Excel 2013 and analysed by using Statistical Package for Social Sciences (SPSS) Version 21. For all statistical analysis, P value< 0.001 was considered as significant.

Results

In our study, 194 out of 320 patients (60.6%) with breast cancer were 40 to 60 years of age. 4 out of 320 patients in the study were males. Left breast carcinoma was slightly higher in prevalence than right breast cancer accounting for 164 patients out of 320 (51.25%). The site of tumor in the breast was most commonly the upper outer quadrant in 148patients (46.25%) (Table 1).

Morphologically, 200 (62.5%) out of 320 patients had gross pathological tumor size ranging from more than 2 cm up to 5 cm. 164 patients (51.3%) had T2 stage tumors and 42 patients (13.1%) presented with skin involvement-mostly skin ulceration and peau d' orange. 160 (50%) patients had no lymph node metastases pathologically (Table 1). 94 of the 320 patients presented with pathological TNM Stage IIA (Figure 1).

Infiltrating ductal carcinoma, not otherwise specified, is the most common histological type of breast tumor encountered in 270 (84.4%) out of 320 patients. Other histological types found were mucinous carcinoma, invasive papillary carcinoma and infiltrating lobular carcinoma. According to the modified Scarff Bloom Richardson scoring, 216 patients (67.5%) had histological grade III tumors. Lymphovascular space invasion was noted in only 42 patients (13.1%). 100 out of 320 patients (31.25%) showed presence of tumor necrosis histopathologically. 68 patients (21.25%) had close or positive postoperative margins (Table 1). In our study, close margin was defined as margin within 5 mm from the tumor. In most of the margin close or involved patients, it was the posterior margin which was affected.

On immunohistochemistry, 180 (56.25%) and 170 (53.1%) patients expressed ER and PR positive tumors respectively (Table 1).

On correlating the study variables with ER and PR status of the patients in the study, we obtained a statistically significant association (p<0.001) between ER, PR status of the tumor with the age of the patient. Also the TNM pathological Stage and histological tumor grade showed significant correlation (p<0.001) with both ER and PR status. (Table 2).

Table 1. Clinical and Morphological Characteristics of Study Population

Variables		Frequency (N=320)	Percentage (%)
Age	<40	82	25.6
	40-60	194	60.6
	>60	44	13.8
Sex	Females	316	98.75
	Males	4	1.25
Tumor Site	Central	64	20
	Upper Outer	148	46.25
	Lower Inner	36	11.25
	Lower Outer	12	3.75
	Upper Inner	60	18.75
Breast Involved	Right	156	48.75
	Left	164	51.25
Tumor Size	≤2 Cm	36	11.3
	>2-5 Cm	200	62.5
	>5 Cm	84	26.2
T Stage	1	32	10
	2	164	51.3
	3	82	25.6
	4	42	13.1
N Stage	N0	160	50
	N1	98	30.6
	N2	26	8.1
	N3	36	11.3
Histological Types	IDC NOS	270	84.4
	IPC	22	6.9
	ILC	22	6.9
	MC	6	1.9
Histological Grade	I	20	6.3
	II	84	26.3
	III	216	67.5
LVSI	Positive	42	13.1
	Negative	278	86.9
Tumor Necrosis	Positive	100	31.25
	Negative	220	68.75
Margin Status	Close/Positive	68	21.25
	Negative	252	78.75
ER Status	Positive	180	56.25
	Negative	140	43.75
PR Status	Positive	170	53.1
	Negative	150	46.9

*LVSI = Lymphovascular space invasion, IDC NOS = Infiltrating ductal carcinoma, not otherwise specified, IPC = Invasive papillary carcinoma, ILC = Infiltrating lobular carcinoma, MC = Mucinous carcinoma

Table 2. Distribution of Study Variables According to ER and PR Status

Variables		ER+VE	ER-VE	p value	PR+VE	PR-VE	p value
Age	≤40	36	46		36	46	
(Years)	>40-60	104	90	<0.001	96	98	<0.001
	>60	140	4		38	6	
Tumor Size	≤2	20	16		18	18	
(Cm)	>2-5	124	76	0.012	114	86	0.179
	>5	36	48		38	46	
pT Stage	1	20	12		18	14	
	2	106	58	0.004	98	66	0.039
	3	36	46		38	44	
	4	18	24		16	26	
pN Stage	0	100	60		92	68	
	1	56	42	0.002	60	38	0.003
	2	6	20		6	20	
	3	18	18		12	24	
TNM Stage	Ia	12	6		10	8	
	IIa	68	26		62	32	
	IIb	44	26	<0.001	50	20	<0.001
	IIIa	22	40		22	40	
	IIIb	16	24		14	26	
	IIIc	18	18		12	24	
Tumor Grade							
	I	16	4		16	4	
	II	72	12	<0.001	66	18	<0.001
	III	92	124		88	128	
LVSI	Positive	24	18	0.9	24	18	0.576
	Negative	156	122		146	132	
Tumor Necrosis							
	Positive	38	62	0.003	46	54	0.085
	Negative	142	78		124	96	

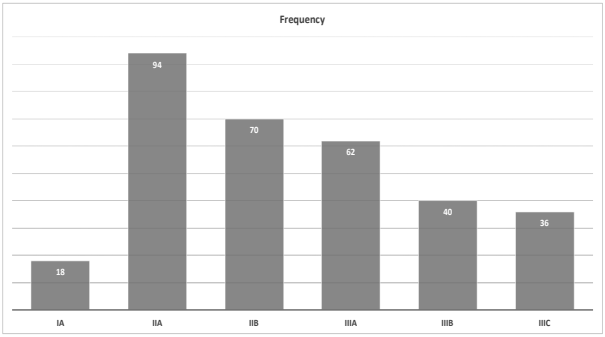

Figure 1. Clustered Column Chart Depicting the Frequency Distribution of Study Population in Various TNM Stages of Breast Cancer

Discussion

Breast cancer is one of the most frequently diagnosed cancer in developed countries (Siegel et al., 2014). But now, breast cancer incidence has been on a rise in developing countries too, especially in urban areas (Murthy et al., 2009).

Most of the patients were in the age group of 40 to 60 years, with a mean age of 51.4 years. The mean age of breast cancer patients in developed countries is almost one decade higher when compared to Indian studies (Stead et al., 2009; Sandhu et al., 2010). On correlating age with ER and PR status, hormone receptor positivity was found to be more common in elderly patients as has been found in literature (Sofi et al., 2012). Men comprise of only around 1% of all diagnosed breast cancers (Sedighi et al., 2013). As found in literature as well as the current study, upper outer quadrant is the most common siteof primary breast tumor (Sofi et al., 2012).

Most common histological type of breast cancer was infiltrating ductal carcinoma similar to that found in literature (Shet et al., 2009; Sofi et al., 2012). Most commonly, the tumors were of 2 to 5 cm in size, as has been also found in other studies (Sofi et al., 2012). 50% patients in the study had lymph nodal involvement on presentation, which indicates the aggressive nature of the tumors found in Indian population. Though data from developed countries suggest that most of the breast cancer patients do not have any lymph node metastasis, Indian studies have documented higher percentages of lymph nodal involvement in breast cancer patients (Taucher et al., 2003; Sofi et al., 2012; Rao et al., 2013). Most of the patients presented in TNM Stage II as most of the patients had tumor size between 2 to 5 cm and 50% of the patients did not have any lymph nodal disease. Both ER and PR status correlated significantly with the stage of the disease, thereby indicating that ER, PR positive tumors were associated with early stage breast tumors. Similar correlation was also found in other studies (Zhou et al., 2014).

An Indian study with 11780 patients of breast cancer, found 70% of the tumors to be of histological grade III (Shet et al., 2009). Similar results were found in the current study. Alike some other studies, the hormone receptor status in the present study significantly correlated with the histological grade of breast tumors (Sofi et al., 2012; Shet et al., 2009; Ambroise et al., 2011). Similar to a regional study, lymphovascular space invasion was seen in less than 20% of the patients (Rao et al., 2013). Presence of histologic tumor necrosis has been found to be higher in Indian studies (Rao et al., 2013).

The prevalence of ER and PR expression on immunohistochemistrywere 56.25% and 53.1% respectively in the present study as opposed to the 75% ER and 58% PR positivity documented in western literature (Rhodes et al., 2000). In India, the prevalence of hormone receptor positivity has been seen to be lower, when compared to western literature (Shet et al., 2009; Ambroise et al., 2011). In a study from Southern India, the prevalence of ER, PR co-positivity was found to be 32% only (Zubeda et al., 2014). An additional HER2/neu testing in South Indian women with breast cancer demonstrated 46% of the breast tumors to be triple negative (Zubeda et al., 2014). Triple negative breast cancers in Asian population were found to be associated with younger age of onset, increasing tumor size, increased prevalence of axillary lymph nodal involvement, higher histological grade of tumor and poor prognosis (Ma et al., 2013; Li et al., 2014).

In conclusion, in context of developing countries like India, breast cancer occurs in younger female when compared to the developed world. The proportion of histological high grade breast tumors, lymph node involvement are also high, when compared to the data from developed nations. Percentage of ER and PR expressing breast tumors is lower when compared to that documented in the western countries.ER, PR negative tumors occur more commonly in young breast cancer patients. ER, PR positive tumors are associated with early stage breast cancers. Lack of expression of ER and PR are also associated with higher histological tumor grades. In developing countries like India, though breast cancer is not yet the most common cancer affecting females, as in the developing countries, breast cancer patients in the developing nations present with more aggressive tumors when compared to that of the west.

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